IN THE UNITED STATES PATENT AND TRADEMARK OFFICE BEFORE THE BOARD OF APPEALS AND INTERFERENCES

Application of: Bazin, et al.

Serial No.: 09/056,072

Filed: April 7, 1998

For: LO-CD2a Antibody and Uses Thereof for Inhibiting T-Cell Activation and Proliferation

Group: 1644

Examiner: Gambel

Assistant Commissioner of Patents
Washington, D.C. 20231

BRIEF BEFORE THE BOARD OF APPEALS AND INTERFERENCES

Sir:

This is an appeal from the Final Rejection dated April 13, 1999.

Status of Claims

Claims 30-44 are pending, stand finally rejected, and are before the Board on appeal. These claims are listed in the Appendix attached hereto.

Status of Amendments

A response to the Final Rejection was filed on October 8, 1999. The claims were not amended in this response.

Real Party in Interest

The real party in interest is the Université Catholique de Louváin, the assignee of the claimed subject matter of the above-identified application.

Related Appeals and Interferences

There are no related appeals and interferences with respect to the above-identified application.

Summary of the Invention

The present invention is directed to an antibody. As defined broadly in Claim 30, the antibody binds to the same epitope on human lymphocytes as the antibody produced by the cell line deposited as ATCC HB11423.

The present invention also is directed to a cell line which, as defined broadly in Claim 35, produces an antibody which binds to the same epitope on human lymphocytes as the antibody produced by the cell line deposited as ATCC HB11423.

In another aspect of the claimed invention, there is provided a composition which as defined broadly in Claim 38, comprises an antibody which binds to the same epitope on human lymphocytes as the antibody produced by the cell line deposited as ATCC HB11423. the composition also comprises a pharmaceutically acceptable carrier. The antibody is present in the composition in an amount effective to inhibit a T-cell mediated immune response.

In yet another aspect of the present invention, there is provided, as defined in Claim 44, a composition which comprises an antibody produced by the cell line deposited as ATCC HB11423. The composition also comprises a pharmaceutically acceptable carrier. The antibody is present in the composition in an amount effective to inhibit a T-cell mediated immune response.

Issues Presented and Grouping of Claims

Claims 30-32, 35-40, and 43 stand rejected under 35 U.S.C. 102(b) as being anticipated by Xia, et al.

It is the Examiner's position that Xia teaches the LO-CD2a specificity, including hybridomas and methods of making the antibodies and hybridomas of the claimed invention. The Examiner also states that although Xia is silent about a pharmaceutically acceptable carrier per se, the storage and use of the LO-CD2a antibody in pharmaceutically acceptable carriers such as PBS was well known, practiced, and envisaged immediately at the time the invention was made in the art. The Examiner also holds that the intended use or amount to elicit alloantigen specific hyporesponsiveness would have been met by Xia as such claimed encompasses a broad range as the amount of antibody to elicit immunosuppression would depend on the nature of the system being analyzed or tested.

Claim 30-43 stand rejected under 35 U.S.C. 103 as being unpatentable over Xia, et al. in view of Queen, et. al. or Newman, et al., and in further view of Guckel, et al. or Bromberg, et. al. or Hafler, et al. or Chavin, et al. or Faustman.

The Examiner states that Xia teaches the LO-CD2a specificity and relies upon a number of characteristics to distinguish this specificity, including distinguishing the LO-CD2a specificity from other CD2 specific antibodies. The Examiner states that while the characteristics disclosed by the prior art may be common to certain classes of CD2 specific antibodies, including providing a number of characteristics and comparisons that would lead to an expectation of success of antibodies that bind the same epitope as the LO-CD2a antibody. The Examiner also states that there is sufficient guidance in Xia to distinguish the LO-CD2a specificity. In addition, the Examiner states that the intended use or amount to elicit alloantigen specific hyporesponsiveness would have been met by the reference as such claimed amounts encompass a broad range as the amount of antibody to elicit the immunosuppression would depend on the nature of the system being analyzed or tested.

The Examiner concludes that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to generate CD2-specific antibodies including the LO-CD2a-specific antibodies to characterize the CD2 specificity and to target the specificity for various biological, diagnostic, and therapeutic modalities. The Examiner states that from the teachings of the references, such was apparent to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Claims 34 and 42 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to point out particularly and claim distinctly the subject matter which Applicants regard as the invention.

The Examiner has taken the position that Claims 34 and 42 are indefinite in the recitation of "chimeric" because the metes and bounds are unclear and that chimeric antibodies can be a broad term that encompasses any number of recombinant forms of antibodies.

The rejected claims do not stand or fall together, for reasons which will be explained hereinbelow.

Argument

Xia, alone or in view of the other cited references, does not render the present claims unpatentable.

During prosecution of parent application Serial No. 08/472,281, now U.S. Patent No. 5,817,311, the Patent Office acknowledged that the antibody produced by such cell line is patentable over the prior art.

The issue remains whether or not one skilled in the art from reading Xia, et al. would be enabled to obtain an antibody which binds to the same epitope as the antibody produced by the deposited cell line.

In support of Applicants' position, Applicants submit herewith a copy of a Declaration by Dr. Barbara E. Bierer, which was filed in parent application Serial No. 08/472,281, now U.S. Patent No. 5,817,311.

Applicants assert that if, as the Patent Office recognized during prosecution of parent application Serial No. 08/472,281, now U.S. Patent No. 5,817,311, one skilled in the art could not produce the deposited antibody, one skilled in the art also would not be enabled by Xia to produce an antibody which binds to the same epitope.

As indicated in the Declaration of Dr. Bierer, the characteristics which are defined in Xia, et al. are not characteristics which define a specific epitope. The characteristics disclosed by Xia are characteristics common to CD2 antibodies as a class. Thus, even if one skilled in the art were able to identify an antibody which had characteristics similar to those of the LO-CD2a antibody disclosed in Xia, et al., such characteristics do not indicate whether or not an antibody binds to the same epitope as the deposited antibody in that such characteristics are those generally possessed by CD2 antibodies.

As indicated in Dr. Bierer's declaration, from the teachings of Xia, one skilled in the art would have no way of knowing which, if any, of the antibodies which would be produced by the general procedure disclosed by Xia, et al. is LO-CD2a or which binds to the same epitope as the antibody of the present invention in that the characteristics disclosed by Xia do not define LO-CD2a uniquely (distinguishing LO-CD2a from CD2 antibodies as a class) or define which antibodies bind to the same epitope as LO-CD2a or deposited antibody.

The claims of the present application are directed to an antibody which binds to the same epitope as the antibody produced by the deposited cell line. In order to negate the patentability of such claims, it is incumbent upon the Patent Office to provide detailed reasons as to why it believes that the characteristics disclosed by Xia uniquely define antibodies which bind to the same epitope as the antibody produced by the deposited cell line, particularly in view of the Declaration of Dr. Bierer, which indicates clearly that the characteristics included in Xia, et al. are characteristics which are known to be present in CD2 antibodies as a class, and do not define whether or not an antibody binds to a particular epitope. In particular, as noted by Dr. Bierer, different antibodies which bind to different epitopes have the characteristics disclosed by Xia and, therefore, such characteristics are not suitable for identifying an antibody as claimed.

In view of the fact that Xia does not disclose or render obvious to one of ordinary skill in the art the antibody produced by the deposited cell line and further in view of the fact that the characteristics disclosed by Xia are not characteristics which are related to a specific epitope, Xia does not disclose or render obvious to one of ordinary skill in the art an antibody which binds to the same epitope as the antibody produced by the deposited cell line.

Although Xia at Page 320 indicates that the LO-CD2a antibody binds to an epitope which is different from other antibodies referred to on Page 320, Xia does not identify the epitope to which LO-CD2a binds. Because Xia does not define the epitope, Xia does not make LO-CD2a available to one skilled in the art, and one skilled in the art would not have sufficient information to determine whether or not a produced antibody bound to the same epitope as LO-CD2a. The information provided on Page 320 at best permits one skilled in the art to determine that a produced antibody is not D66. Such information does not enable one to determine whether a produced antibody is LO-CD2a, or an antibody other than LO-CD2a.

In addition, the prior art does not provide any reasonable expectation that the claimed antibody or a composition including such antibody in combination with a pharmaceutically acceptable carrier could be used successfully in a human. In fact, the prior art as a whole suggests that CD2 antibodies would not be successful.

In this respect, Thurlow et al. (Transplantation, Vol. 36, pages 293-97), copy attached, reports that an attempt to use a CD2 monoclonal antibody in a human was not successful.

Giorgi (Transplantation Proceedings, Vol. 15) reports that another CD2 antibody was not successful in primate studies.

Thus, there is nothing in the prior art which would lead one to expect that the claimed compound could be used in treating patients.

The Examiner's attention is drawn to Pages 40-43 of the Specification which provides human data. It is noted that the human data shows successful treatment after onset of rejection; *i.e.*, the treatment can reverse rejection.

This should be contrasted with the indication in the prior art that CD2 antibodies if effective at all would be effective only if administered immediately after T-cell priming (Guckel, Page 964, Paragraph bridging Col. 1 and 2).

As the Examiner was aware, in treating rejection or other T-cell mediated responses, it is virtually impossible to treat within 24 hours of antigen "priming."

Thus, the ability to treat patients successfully in accordance with the invention would not be expected from the prior art. In fact, the prior art suggests that CD2 antibodies would not be suitable for the treatment of patients.

The claimed subject matter is directed to an antibody which binds to the same epitope as the antibody produced by the deposited cell line. The totality of the evidence, including the

Declaration of Dr. Bierer, indicates that the characteristics disclosed by Xia, et al. are not sufficient to identify LO-CD2a in a manner which distinguishes LO-CD2a from CD2 antibodies as a class or to enable one skilled in the art to identify antibodies which bind to the same epitope as the antibody produced by the deposited cell line.

In addition, Applicants have found unexpectedly that the claimed antibody may be employed to treat humans, contrary to the accepted wisdom of the prior art. Such findings, therefore, are a clear indication of the nonobviousness of the claimed antibody as employed in combination with an acceptable pharmaceutical carrier for treating humans. (See W.L. Gore and Associates, Inc. v. Garlock Inc., 220 U.S.P.Q. 303 (C.A.F.C. 1983), at 312; United States v. Adams, 383 U.S. 39 (1966)).

Also, because the prior art does not disclose or even remotely suggest to one of ordinary skill in the art that the claimed antibody may be used to treat humans, the cited prior art does not render obvious to one of ordinary skill in the art the combination of the claimed antibody and an acceptable pharmaceutical carrier, as defined in Claim 38, even if, assuming solely for the sake of argument, the claimed antibody were known. (See Ex Parte Erdmann, 194 U.S.P.Q. 96 (Bd. App. 1976), at 97.) The prior art, therefore, provides no basis for the claimed invention, and does not render the claimed invention obvious to one of ordinary skill in the art within the meaning of 35 U.S.C. 103.

With respect to the rejection of Claims 34 and 42, under 35 U.S.C. 112, second paragraph, although the term "chimeric" may include a variety of antibodies, such term is well known to those skilled in the art, and therefore such term does not render the claims indefinite. One skilled in the art could determine readily whether a particular antibody is a chimeric antibody and whether such an antibody binds to the same epitope on human lymphocytes as the

antibody produced by the deposited cell line, and thus infringe Claims 34 and/or 42. For the above reasons and others, Claims 34 and 42 are not indefinite, and it is therefore respectfully requested that the rejection under 35 U.S.C. 112, second paragraph, be reversed.

For the above reasons and others, this application is in condition for allowance, and it is respectfully requested that the rejections be reversed.

Respectfully submitted,

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(Date of Deposit)
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Signature
4/5/2000
Date of Signature

APPENDIX - CLAIMS ON APPEAL

30. An antibody which binds to the same epitope on human lymphocytes as the antibody produced by the cell line deposited as ATCC HB 11423.

31. The antibody of Claim 30 wherein the antibody is a monoclonal antibody.

32. The antibody of Claim 31 wherein the antibody is a rat antibody.

33. The antibody of Claim 31 wherein the antibody is a humanized form of said antibody.

34. The antibody of Claim 31 wherein the antibody is a chimeric form of said antibody.

35. A cell line which produces an antibody which binds to the same epitope on human lymphocytes as the antibody produced by the cell line deposited as ATCC HB 11423.

36. A process for producing an antibody comprising:

producing an antibody by culturing the cell line of Claim 35.

37. The antibody of Claim 31 wherein said antibody elicits alloantigen specific hyporesponsiveness.

38. A composition, comprising:

(a) an antibody which binds to the same epitope on human lymphocytes as the antibody produced by the cell line deposited as ATCC HB 11423; and

(b) a pharmaceutically acceptable carrier, wherein said antibody is present in said composition in an amount effective to inhibit a T-cell mediated immune response.

39. The composition of Claim 38 wherein the antibody is a monoclonal antibody.

40. The composition of Claim 39 wherein the antibody is a rat antibody.

41. The composition of Claim 39 wherein the antibody is a humanized form of said antibody.

42. The antibody of Claim 39 wherein the antibody is a chimeric form of said antibody.

43. The composition of Claim 38 wherein said antibody is present in said composition in an amount effective to elicit alloantigen specific hyporesponsiveness.

44. A composition, comprising:

(a) an antibody produced by the cell line deposited as ATCC HB11423; and

(b) a pharmaceutically acceptable carrier, wherein said antibody is present in said composition in an amount effective to inhibit a T-cell mediated immune response.